I claim:

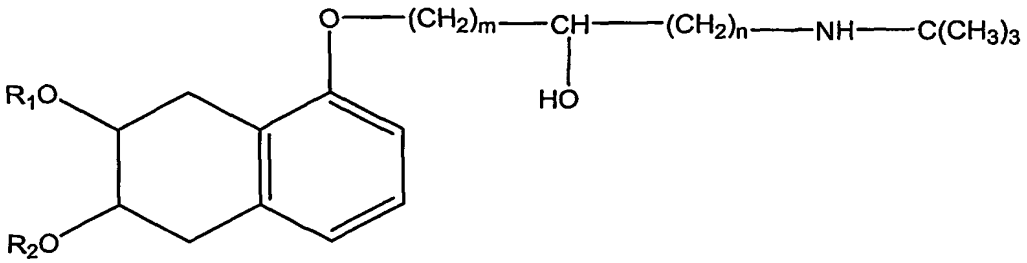
1. A method for treatment of pulmonary airway disease in a subject suffering from pulmonary airway disease comprising administering a therapeutically effective amount of a β-adrenergic inverse agonist to the subject to treat the pulmonary airway disease.

2. The method of claim 1 wherein the β-adrenergic inverse agonist is selected from the group consisting of β_2-selective inverse agonists, and non-selective inverse agonists having inverse agonist activity against both β_1- and β_2-adrenergic receptors.

3. The method of claim 2 wherein the β-adrenergic inverse agonist is a β_2-selective inverse agonist.

4. The method of claim 1 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, and timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

5. The method of claim 4 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol and a compound of formula (I)

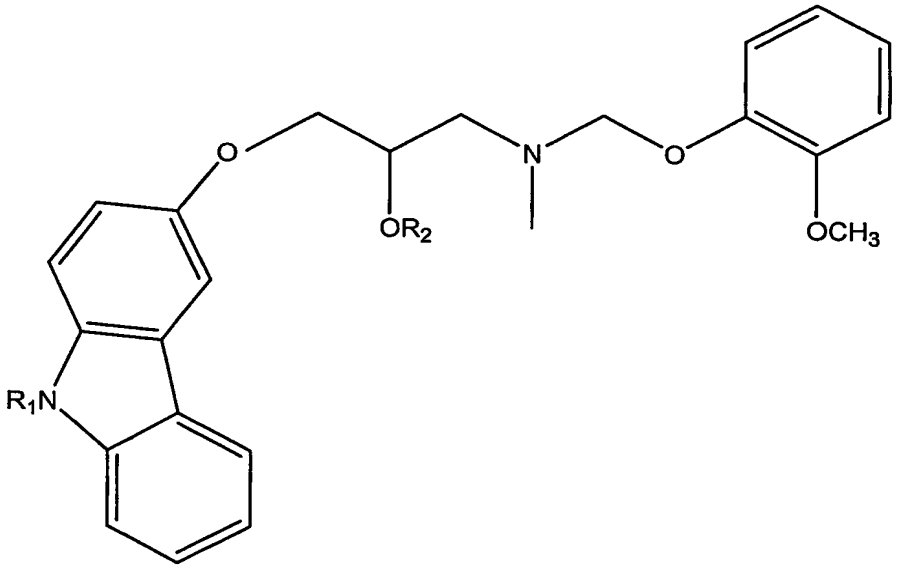


(I)

wherein R_1 is hydrogen or lower alkyl, R_2 is hydrogen or lower alkyl, and m and n are 1 to 3, with the proviso that where R_1 and R_2 are both hydrogen and m is 1, n is other than 1.

6. The method of claim 5 wherein the β-adrenergic inverse agonist is nadolol.

7. The method of claim 4 wherein the β-adrenergic inverse agonist is selected from the group consisting of carvedilol and a compound of formula (II)

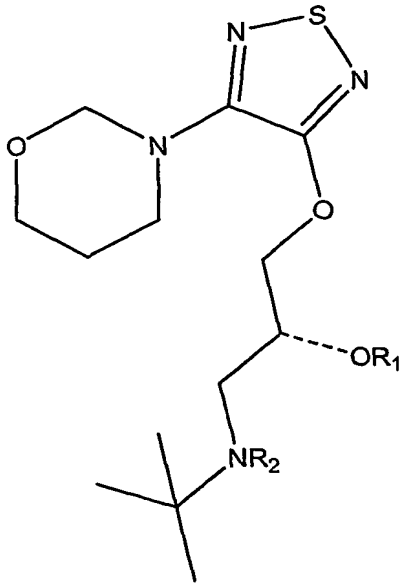


(II)

wherein R_1 is hydrogen or lower alkyl, R_2 is hydrogen or lower alkyl, and R_3 is hydrogen or lower alkyl, with the proviso that all of R_1, R_2, and R_3 are not all hydrogen.

8. The method of claim 7 wherein the β-adrenergic inverse agonist is carvedilol.

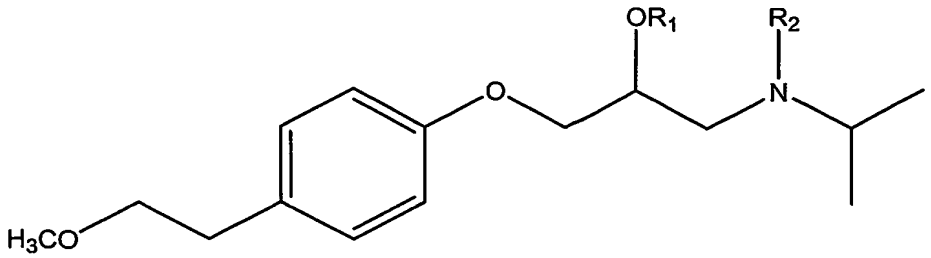
9. The method of claim 1 wherein the β-adrenergic agonist is selected from the group consisting of timolol and analogues of timolol of formula (III) wherein R_1 is hydrogen or lower alkyl and R_2 is hydrogen or lower alkyl, with the proviso that both R_1 and R_2 are not hydrogen.



(III)

10. The method of claim 9 wherein the β-adrenergic inverse agonist is timolol.

11. The method of claim 1 wherein the β-adrenergic agonist is selected from the group consisting of metoprolol and analogues of metoprolol of formula (IV) wherein R_1 is hydrogen or lower alkyl and R_2 is hydrogen or lower alkyl, with the proviso that both R_1 and R_2 are not hydrogen.



(IV)

12. The method of claim 11 wherein the β-adrenergic inverse agonist is metoprolol.

13. The method of claim 1 wherein the method exerts a therapeutic effect that is a reduction in pulmonary airway constriction hyperresponsiveness.

14. The method of claim 1 wherein the method exerts a therapeutic effect that is an up regulation of pulmonary β_2-adrenergic receptors.

15. The method of claim 1 wherein the method exerts a therapeutic effect that is increased pulmonary airway relaxation responsiveness to β_2-adrenergic agonist drugs.

16. The method of claim 1 wherein the β-adrenergic inverse agonist is administered by a route selected from the group consisting of oral, sustained-release oral, parenteral, sublingual, buccal, insufflation, and inhalation.

17. The method of claim 16 wherein the β-adrenergic inverse agonist is administered by the sustained-release oral route.

18. The method of claim 1 wherein the pulmonary airway disease is selected from the group consisting of asthma, bronchiectasis, bronchitis,

chronic obstructive pulmonary disease, Churg-Strauss syndrome, pulmonary sequelae of cystic fibrosis, emphysema, allergic rhinitis, and pneumonia.

19. The method of claim 18 wherein the pulmonary airway disease is asthma.

20. The method of claim 18 wherein the pulmonary airway disease is chronic obstructive pulmonary disease.

21. The method of claim 18 wherein the pulmonary airway disease is emphysema.

22. The method of claim 1 wherein the subject is a human.

23. The method of claim 1 wherein the subject is a socially or economically important animal selected from the group consisting of a dog, a cat, a horse, a sheep, a goat, and a pig.

24. The method of claim 1 wherein the method of administration of the β-adrenergic inverse agonist results in continuous levels of the β_2-adrenergic inverse agonist in the bloodstream of the subject.

25. The method of claim 1 wherein the β-adrenergic inverse agonist is administered over time in a series of graduated doses starting with the lowest dose and increasing to the highest dose.

26. The method of claim 25 wherein, when the highest dose is reached, the β-adrenergic inverse agonist continues to be administered at that dose.

27. A pharmaceutical composition comprising:

(a) nadolol in a quantity selected from the group consisting of 1 mg, 3 mg, 5, mg, 10 mg, 15 mg, 30 mg, 50 mg, and 70 mg; and

(b) a pharmaceutically acceptable carrier.

28. A blister pack comprising:

(a) a lower substrate;

(b) an intermediate dosage holder that is shaped to generate a plurality of cavities and that is placed over the lower substrate, the cavities being shaped to hold dosage forms of a β-adrenergic inverse agonist;

(c) an upper substrate placed over the intermediate dosage holder that has a plurality of apertures, each aperture being located to accommodate a corresponding cavity; wherein the dosage forms are of graduated dosages starting with a lowest dose and proceeding to a highest dose; and

(d) dosage forms of a β-adrenergic inverse agonist placed in the cavities.

29. The blister pack of claim 28 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

30. The blister pack of claim 28 wherein the β-adrenergic inverse agonist is nadolol.

31. The blister pack of claim 28 wherein the β-adrenergic inverse agonist is carvedilol.

32. A blister pack comprising:

(a) a lower substrate;

(b) an intermediate dosage holder that is shaped to generate a plurality of cavities, the cavities being shaped to hold dosage forms of a β-adrenergic inverse agonist;

(c) an upper substrate placed over the intermediate dosage holder that has a plurality of apertures, each aperture being located to accommodate a corresponding cavity; and

(d) dosage forms of a β-adrenergic inverse agonist placed in the cavities, wherein the dosage forms are of at least two dosages of a β-adrenergic inverse agonist: (i) a maintenance dose that is the highest dose in a series of graduated doses; and (ii) at least one backup restoration dose or a lower dose to be taken in a specified condition.

33. The blister pack of claim 28 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

34. The blister pack of claim 33 wherein the β-adrenergic inverse agonist is nadolol.

35. The blister pack of claim 33 wherein the β-adrenergic inverse agonist is carvedilol.

36. The blister pack of claim 33 wherein the blister pack comprises at least one backup restoration dose.

37. The blister pack of claim 33 wherein the blister pack comprises at least one lower dose to be taken in a specified condition.

38. The blister pack of claim 37 wherein the specified condition is the administration of an antibiotic that affects the catabolism of the β-adrenergic inverse agonist.

39. The blister pack of claim 38 wherein the antibiotic is selected from the group consisting of erythromycin and neomycin.

40. A method for treatment of pulmonary airway disease in a subject suffering from pulmonary airway disease comprising administering to the subject: (1) a therapeutically effective amount of a β-adrenergic inverse agonist and (2) a therapeutically effective amount of a β_2-selective adrenergic agonist in order to treat the pulmonary airway disease.

41. The method of claim 40 wherein the β_2-selective adrenergic agonist is selected from the group consisting of albuterol, bitolterol, clenbuterol, clorprenaline, dobutamine, fenoterol, formoterol, isoetharine, isoprenaline, levabuterol, mabuterol, metaproterenol, pirbuterol, ritodrine, salbutamol, salmeterol, terbutaline, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

42. The method of claim 40 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

43. The method of claim 42 wherein the β-adrenergic inverse agonist is nadolol.

44. The method of claim 42 wherein the β-adrenergic inverse agonist is carvedilol.

45. The method of claim 40 wherein the pulmonary airway disease is selected from the group consisting of asthma, bronchiectasis, bronchitis, chronic obstructive pulmonary disease, Churg-Strauss syndrome, pulmonary sequelae of cystic fibrosis, emphysema, allergic rhinitis, and pneumonia.

46. The method of claim 45 wherein the pulmonary airway disease is asthma.

47. The method of claim 45 wherein the pulmonary airway disease is chronic obstructive pulmonary disease.

48. A method for treatment of pulmonary airway disease in a subject suffering from pulmonary airway disease comprising administering to the subject: (1) a therapeutically effective amount of a β-adrenergic inverse agonist and (2) a therapeutically effective amount of a steroid in order to treat the pulmonary airway disease.

49. The method of claim 48 wherein the steroid is selected from the group consisting of beclomethasone, budenoside, ciclesonide, flunisolide, fluticasone, methylprednisolone, prednisolone, prednisone, and triamcinolone, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

50. The method of claim 48 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

51. The method of claim 50 wherein the β-adrenergic inverse agonist is nadolol.

52. The method of claim 50 wherein the β-adrenergic inverse agonist is carvedilol.

53. The method of claim 44 wherein the pulmonary airway disease is selected from the group consisting of asthma, bronchiectasis, bronchitis, chronic obstructive pulmonary disease, Churg-Strauss syndrome, pulmonary sequelae of cystic fibrosis, emphysema, allergic rhinitis, and pneumonia.

54. The method of claim 53 wherein the pulmonary airway disease is asthma.

55. The method of claim 53 wherein the pulmonary airway disease is chronic obstructive pulmonary disease.

56. A method for treatment of pulmonary airway disease in a subject suffering from pulmonary airway disease comprising administering to the subject: (1) a therapeutically effective amount of a β-adrenergic inverse agonist and (2) a therapeutically effective amount of an anticholinergic drug in order to treat the pulmonary airway disease.

57. The method of claim 56 wherein the anticholinergic drug is selected from the group consisting of ipratropium bromide, tiotropium bromide, and oxitropium bromide, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

58. The method of claim 56 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine,

carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

59. The method of claim 58 wherein the β-adrenergic inverse agonist is nadolol.

60. The method of claim 58 wherein the β-adrenergic inverse agonist is carvedilol.

61. The method of claim 52 wherein the pulmonary airway disease is selected from the group consisting of asthma, bronchiectasis, bronchitis, chronic obstructive pulmonary disease, Churg-Strauss syndrome, pulmonary sequelae of cystic fibrosis, emphysema, allergic rhinitis, and pneumonia.

62. The method of claim 61 wherein the pulmonary airway disease is asthma.

63. The method of claim 61 wherein the pulmonary airway disease is chronic obstructive pulmonary disease.

64. A method for treatment of pulmonary airway disease in a subject suffering from pulmonary airway disease comprising administering to the subject: (1) a therapeutically effective amount of a β-adrenergic inverse agonist and (2) a therapeutically effective amount of a xanthine compound in order to treat the pulmonary airway disease.

65. The method of claim 64 wherein the xanthine compound is selected from the group consisting of theophylline, extended-release theophylline, aminophylline, theobromine, enprofylline, diprophylline, isbufylline, choline theophyllinate, albifylline, arofylline, bamifylline and caffeine.

66. The method of claim 64 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

67. The method of claim 66 wherein the β-adrenergic inverse agonist is nadolol.

68. The method of claim 66 wherein the β-adrenergic inverse agonist is carvedilol.

69. The method of claim 64 wherein the pulmonary airway disease is selected from the group consisting of asthma, bronchiectasis, bronchitis, chronic obstructive pulmonary disease, Churg-Strauss syndrome, pulmonary sequelae of cystic fibrosis, emphysema, allergic rhinitis, and pneumonia.

70. The method of claim 69 wherein the pulmonary airway disease is asthma.

71. The method of claim 69 wherein the pulmonary airway disease is chronic obstructive pulmonary disease.

72. A method for treatment of pulmonary airway disease in a subject suffering from pulmonary airway disease comprising administering to the subject: (1) a therapeutically effective amount of a β-adrenergic inverse agonist and (2) a therapeutically effective amount of an anti-IgE antibody in order to treat the pulmonary airway disease.

73. The method of claim 72 wherein the anti-IgE antibody is a monoclonal antibody or a genetically engineered antibody that is derived from a monoclonal antibody.

74. The method of claim 73 wherein the anti-IgE antibody is humanized.

75. The method of claim 74 wherein the humanized antibody is an IgG1 κ monoclonal antibody.

76. The method of claim 75 wherein the IgG1 κ monoclonal antibody is omalizumab.

77. The method of claim 72 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

78. The method of claim 77 wherein the β-adrenergic inverse agonist is nadolol.

79. The method of claim 77 wherein the β-adrenergic inverse agonist is carvedilol.

80. The method of claim 72 wherein the pulmonary airway disease is selected from the group consisting of asthma, bronchiectasis, bronchitis, chronic obstructive pulmonary disease, Churg-Strauss syndrome, pulmonary sequelae of cystic fibrosis, emphysema, allergic rhinitis, and pneumonia.

81. The method of claim 80 wherein the pulmonary airway disease is asthma.

82. The method of claim 80 wherein the pulmonary airway disease is chronic obstructive pulmonary disease.

83. A method for treatment of pulmonary airway disease in a subject suffering from pulmonary airway disease comprising administering to the subject: (1) a therapeutically effective amount of a β-adrenergic inverse agonist and (2) a therapeutically effective amount of a leukotriene modifier in order to treat the pulmonary airway disease.

84. The method of claim 83 wherein the leukotriene modifier is selected from the group consisting of ibudilast, montelukast, pranlukast, and zafirlukast, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

85. The method of claim 83 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

86. The method of claim 85 wherein the β-adrenergic inverse agonist is nadolol.

87. The method of claim 85 wherein the β-adrenergic inverse agonist is carvedilol.

88. The method of claim 83 wherein the pulmonary airway disease is selected from the group consisting of asthma, bronchiectasis, bronchitis,

chronic obstructive pulmonary disease, Churg-Strauss syndrome, pulmonary sequelae of cystic fibrosis, emphysema, allergic rhinitis, and pneumonia.

89. The method of claim 88 wherein the pulmonary airway disease is asthma.

90. The method of claim 88 wherein the pulmonary airway disease is chronic obstructive pulmonary disease.

91. A method for treatment of pulmonary airway disease in a subject suffering from pulmonary airway disease comprising administering to the subject: (1) a therapeutically effective amount of a β-adrenergic inverse agonist and (2) a therapeutically effective amount of a phosphodiesterase IV inhibitor in order to treat the pulmonary airway disease.

92. The method of claim 91 wherein the phosphodiesterase IV inhibitor is selected from the group consisting of roflumilast and cilomilast, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

93. The method of claim 91 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

94. The method of claim 93 wherein the β-adrenergic inverse agonist is nadolol.

95. The method of claim 93 wherein the β-adrenergic inverse agonist is carvedilol.

96. The method of claim 91 wherein the pulmonary airway disease is selected from the group consisting of asthma, bronchiectasis, bronchitis, chronic obstructive pulmonary disease, Churg-Strauss syndrome, pulmonary sequelae of cystic fibrosis, emphysema, allergic rhinitis, and pneumonia.

97. The method of claim 96 wherein the pulmonary airway disease is asthma.

98. The method of claim 96 wherein the pulmonary airway disease is chronic obstructive pulmonary disease.

99. A pharmaceutical composition comprising:

(a) a therapeutically effective amount of a β-adrenergic inverse agonist;

(b) a therapeutically effective amount of a second therapeutic agent effective to treat a pulmonary airway disease, the second therapeutic agent being selected from the group consisting of a β_2-selective adrenergic agonist, a steroid, an anticholinergic drug, a xanthine compound, an anti-IgE antibody, a leukotriene modifier, and a phosphodiesterase IV inhibitor; and

(c) a pharmaceutically acceptable carrier.

100. The pharmaceutical composition of claim 99 wherein the β-adrenergic inverse agonist is selected from the group consisting of nadolol, bupranolol, butoxamine, carazolol, carvedilol, ICI-118,551, levobunolol, metoprolol, propranolol, sotalol, timolol, and the salts, solvates, analogues, congeners, bioisosteres, hydrolysis products, metabolites, precursors, and prodrugs thereof.

101. The pharmaceutical composition of claim 99 wherein the β-adrenergic inverse agonist is nadolol.

102. The pharmaceutical composition of claim 99 wherein the β-adrenergic inverse agonist is carvedilol.

103. A blister pack comprising:

(a) a lower substrate;

(b) an intermediate dosage holder that is shaped to generate a plurality of cavities and that is placed over the lower substrate, the cavities being shaped to hold dosage forms of the pharmaceutical composition of claim 99;

(c) an upper substrate placed over the intermediate dosage holder that has a plurality of apertures, each aperture being located to accommodate a corresponding cavity; and

(d) dosage forms of the pharmaceutical composition placed in the cavities.

104. The blister pack of claim 99 wherein the dosage forms of the pharmaceutical composition include graduated dosages of the β-adrenergic inverse agonist of the pharmaceutical composition starting with a lowest dose of the β-adrenergic inverse agonist and proceeding to a highest dose of the β-adrenergic inverse agonist.

105. A blister pack comprising:

(a) a lower substrate;

(b) an intermediate dosage holder that is shaped to generate a plurality of cavities and that is placed over the lower substrate, the cavities being shaped to hold dosage forms of: (i) a first pharmaceutical composition that comprises: (A) a therapeutically effective amount of a β-adrenergic inverse agonist; and (B) a first pharmaceutically acceptable carrier; and (ii) a second pharmaceutical composition that comprises: (A) a therapeutically effective amount of a second therapeutic agent effective to treat a pulmonary airway disease, the second therapeutic agent being selected from the group consisting

of a β_2-selective adrenergic agonist, a steroid, an anticholinergic drug, a xanthine compound, an anti-IgE antibody, a leukotriene modifier, and a phosphodiesterase IV inhibitor; and (B) a second pharmaceutically acceptable carrier;

(c) an upper substrate placed over the intermediate dosage holder that has a plurality of apertures, each aperture being located to accommodate a corresponding cavity; and

(d) dosage forms of the first and second pharmaceutical compositions placed in the cavities.

106. The blister pack of claim 105 wherein the dosage forms of the first pharmaceutical composition include graduated dosages of the β-adrenergic inverse agonist of the first pharmaceutical composition starting with a lowest dose of the β-adrenergic inverse agonist and proceeding to a highest dose of the β-adrenergic inverse agonist.